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Patient-related factors may affect the outcome of neuropsychological rehabilitation in multiple sclerosis

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ABSTRACT

Objective: The aim of this study was to identify factors associated with neuropsychological rehabilitation outcome in patients with multiple sclerosis (MS).
Methods: Ninety-eight relapsing–remitting MS patients received multimodal neuropsychological intervention (attention retraining, teaching compensatory strategies, psychoeducation, psychological support, and homework assignments) conducted once a week in 60-minute sessions during thirteen consecutive weeks. The evaluated factors included: 1) patient-related (baseline objective and subjective cognitive performance, mood, fatigue, as well as demographic factors); 2) illness-related (duration and severity of the disease); and 3) intervention-related factors (amount of computer-based attention exercises and homework assignments, therapist's evaluation of the benefit, and therapist).
Results: Patient-related factors affected rehabilitation outcome, whereas illness- and intervention-related factors did not. The results showed that especially MS patients with male gender and more severe attentional deficits benefitted from the intervention.
Conclusion: Patient-related factors may affect neuropsychological rehabilitation outcome in MS.

1. Introduction

Multiple sclerosis (MS) is both an inflammatory and a neurodegenerative disease, with cognition affected in about 50–60% of patients [1,2]. Cognitive impairment is heterogeneous among patients, with impairments in information-processing speed, memory, executive skills and complex attention being the most frequent [1,2]. Cognitive deficits have been demonstrated at all stages and in all subtypes of the disease [2]. Especially, early age at onset, male gender, secondary progressive course, neurodegeneration as indicated by grey matter atrophy, and low average or inferior intelligence (low cognitive reserve) have been suggested to be risk factors for cognitive impairment in MS [3]. Additionally, clinically significant depression or fatigue may aggravate cognitive symptoms [4].

Cognitive impairment detrimentally affects many aspects of daily life, such as the ability to participate fully in society and to maintain employment, with a consequent negative impact on the overall quality of life [2]. Therefore, it is essential that cognitive deficits are taken into account in the treatment and rehabilitation regimen in MS. However, no effective pharmacological treatment for cognitive dysfunction has been established to date [5]. Systematic reviews indicate a low level of evidence for the positive effects of neuropsychological and cognitive rehabilitation in MS [6–8].

Identification of the factors associated with a successful intervention outcome can help to refine the treatments and guarantee a more successful implementation of neuropsychological intervention programmes in the area of treatment services. This could help to focus on limited resources especially to those patients who need and can benefit from the interventions. Overall, the factors contributing to the neuropsychological rehabilitation outcome are largely unknown. Additional research has been called for to investigate the patient characteristics that influence treatment effectiveness [9]. In our previous study, we found that short-term strategy-oriented neuropsychological rehabilitation has positive effects on perceived cognitive deficits as evaluated with the Perceived Deficits Questionnaire (PDQ) in MS [10]. The aim of the present study was to evaluate more closely factors related to the rehabilitation outcome. The evaluated factors were: 1) patient-related factors (baseline objective and subjective cognitive performance, mood, fatigue, and demographic factors); 2) illness-related factors (duration and severity of the disease); and 3) intervention-related factors (amount of computer-based exercises and homework assignments, therapist's evaluation of the patient benefit, and therapist).

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2. Materials and methods

2.1. Patients

Complete details of the study procedure, the patients included, the intervention, and the outcome measures employed are described in our previous publication [10]. Briefly, a total of 102 patients with clinically definite [11] relapsing–remitting multiple sclerosis from three different study centres were included in the study. The patients were randomised into two groups and 98 patients (intervention group 58, control group 40) completed the whole study. There were no significant differences between the intervention and the control group in any of the demographic or clinical background variables (Table 1). The inclusion criteria were clinically definite relapsing–remitting MS, the Expanded Disability Status Scale (EDSS [12]) < 6, subjective deficits in attention (total score of questions 1, 2, and 11 in Multiple Sclerosis Neuropsychological Questionnaire — Patient, MSNQ-P ≥ 6), objective deficits in attention (Symbol Digit Modalities Test, SDMT total score of ≤50), and age 18–59 years. Patients with a history of drug or alcohol abuse, psychiatric disorder, acute relapses, neurological disease other than MS, or ongoing neuropsychological rehabilitation were excluded. To verify the information obtained from the patients regarding their past medical history, hospital records were examined as required. All patients provided written informed consent, and the study protocol was approved by the Ethics Committee of Seinäjoki Central Hospital, Tampere University Hospital and Turku University Hospital.

2.2. Intervention

All patients in the intervention group received outpatient neuropsychological rehabilitation focusing on attentional functions conducted once a week in 60-minute sessions during thirteen consecutive weeks. Co-interventions were avoided in the trial design. Compliance with the intervention was 94.1%. The rehabilitation consisted of computer-based attention and working memory retraining, teaching compensatory strategies, psychoeducation, and homework assignments related to rehabilitation goals, as well as psychological support offered to promote coping with cognitive impairments. The main aim of the strategy-oriented neuropsychological intervention was to support the management of cognitive impairments. The rehabilitation neuropsychologists ($n = 3$) were not the same as the assessing neuropsychologists ($n = 3$). Patients in the control group did not receive any intervention except feedback after their last neuropsychological assessment.

Table 1
Demographic, clinical and behavioural characteristics of the study population at baseline.

Descriptive variables	Intervention ($n = 58$)		Control ($n = 40$)		
	Mean	SD	Mean	SD	p
Demographics					
Age in years	43.5	8.7	44.1	8.8	0.743
Sex, female/male	45/13		31/9		1.000
Education in years	13.6	2.3	13.8	2.6	0.833
Clinical					
EDSS, n/%					
0–4	54/93.1		37/92.5		1.000
4.5–5.5	4/6.9		3/7.5		
Duration since MS diagnosis in years	9.2	6.6	10.1	7.1	0.517
Cognitive performance					
SDMT, total correct	46.3	9.8	45.5	8.4	0.671
BRBNT composite (Z-score)	−0.6	1.2	−1.0	0.8	0.041
Self-reported symptoms/deficits					
PDQ, total score	36.1	11.9	38.2	12.6	0.418
MSNQ-P, total score	28.7	9.2	32.5	9.3	0.046
MSNQ-P attention, sum of questions 1, 2, 11	7.3	1.9	8.1	2.2	0.043
BDI-II, total score	12.8	7.1	10.8	6.3	0.142
MSIS-psychological, composite score	31.5	19.7	28.6	15.7	0.439
FSMC, total score	65.1	17.9	68.1	15.2	0.393

EDSS = Expanded Disability Status Scale; SDMT = Symbol Digit Modalities Test; BRBNT = Brief Repeatable Battery of Neuropsychological tests; PDQ = Perceived Deficits Questionnaire; MSNQ-P = Multiple Sclerosis Neuropsychological Questionnaire – Patient; BDI-II = Beck Depression Inventory II; MSIS-psychological = Multiple Sclerosis Impact Scale – Psychological composite; FSMC = Fatigue Scale for Motor and Cognitive Fatigue.

2.3. Outcome measures

The neuropsychological assessments were performed at baseline, after three months (end of intervention) and after six months, with the timing being similar for all the patients. The assessing neuropsychologists were blind to group membership. Attention, speed of processing, mental flexibility, executive functions, and verbal and visuospatial learning, as well as delayed recall and semantic retrieval were evaluated with the Brief Repeatable Battery of Neuropsychological Tests (BRBNT) [13].

The self-perceived cognitive deficits were evaluated with the Perceived Deficits Questionnaire (PDQ) [14]. The self-reported subjective cognitive symptoms were assessed with the Multiple Sclerosis Neuropsychological Questionnaire (MSNQ-P) [15]. The sum of the answers to questions 1, 2, and 11 in the MSNQ-P served as a measure of subjective attentional deficits. The self-perceived depressive symptoms were evaluated with the Beck Depression Inventory II (BDI-II) [16]. The physical and psychological impact of the disease was assessed with the Multiple Sclerosis Impact Scale (MSIS-29) [17]. Because of the characteristics of the evaluated intervention, only the psychological impact dimension of the scale was analysed. Self-perceived feelings of fatigue were assessed with the Fatigue Scale for Motor and Cognitive Fatigue (FSMC) [18]. Amount of homework assignments was scored on a three-point scale: 1) 0–30%, 2) 31–70%, and 3) 71–100% of given assignments carried out. Additionally, therapists evaluated the benefit of the intervention to the patient on a four-point scale: 1) not at all, 2) to some extent, 3) moderately, and 4) obviously, after the intervention but before knowing the results of the neuropsychological assessment.

2.4. Data analyses

In order to obtain a global cognitive performance score and determine the severity of cognitive impairment, the BRBNT composite score was calculated using the formula suggested by Sepulcre et al. [19] To obtain Z-scores for each cognitive domain in the BRBNT, the reference group of 24 healthy controls was used [20]. Statistical comparisons between the two groups were computed using Fisher's exact tests for nominal data, the Mann–Whitney U-tests for non-normally distributed data and Student's t-tests for normally distributed data.

A linear regression analysis was used to predict the primary rehabilitation outcome, the change in the PDQ, between the first (baseline) and the third (six months) assessment. Patient-related predictors included in addition to group (intervention vs. control), baseline objective (SDMT, BRBNT) and subjective cognitive performance (PDQ, MSNQ-P, MSNQ-P-att), mood (BDI-II), fatigue (FSMC), psychological burden of the disease (MSIS-psyc), age, and years of education. Illness-related predictors included in addition to group, duration (years from diagnosis) of the disease. All the independent variables were tested by linear regression analysis together with the group. The effect of gender and severity of the disease (EDSS) on rehabilitation outcome was evaluated with Student's t-tests within the groups. Intervention-related factors were evaluated with Pearson's correlation analysis and with one-way analysis of variance (ANOVA) when three groups were compared.

To examine the role of the severity of attentional deficits on rehabilitation outcomes more widely, the change between the first (baseline) and the third (six months) assessment in PDQ, MSNQ-P, MSNQ-P-att, BDI-II, MSIS-psyc, and FSMC were compared between the patients with mild and those with moderate to severe attentional deficits separately within the intervention and the control group. The patients